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## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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|--|-----------|---|
| <b>(51) International Patent Classification <sup>6</sup> :</b><br><b>C07D 213/30, 213/32, 403/06, A61K 31/44</b>   | <b>A3</b> | <b>(11) International Publication Number:</b> <b>WO 98/04528</b><br><b>(43) International Publication Date:</b> 5 February 1998 (05.02.98)  |
| <b>(21) International Application Number:</b> PCT/US97/13248<br><b>(22) International Filing Date:</b> 29 July 1997 (29.07.97)<br><b>(30) Priority Data:</b><br>08/690,111 31 July 1996 (31.07.96) US<br><b>(71) Applicants:</b> BAYER CORPORATION [US/US]; 100 Bayer Road, Pittsburgh, PA 15205 (US). BAYER AKTIENGESELLSCHAFT [DE/DE]; D-51368 Leverkusen (DE).<br><b>(72) Inventors:</b> SCHMIDT, Gunter; Pahlkestrasse 63, D-42115 Wuppertal (DE). ANGERBAUER, Rolf; Moospfad 20, D-42113 Wuppertal (DE). BRANDES, Arndt; Pahlkestrasse 5, D-42115 Wuppertal (DE). MULLER-GLIEMANN, Matthias; Holz 24, D-42719 Solingen (DE). BISCHOFF, Hilmar; Am Rohm 78, D-42113 Wuppertal (DE). SCHMIDT, Delf; Am Eckbusch 55b, D-42113 Wuppertal (DE). WOHLFEIL, Stefan; Dorothea-Erxleben-Strasse 31, D-40721 Hilden (DE). SCHOEN, William, R.; 60 Field Brook Road, Madison, CT 06443 (US). LADOUCEUR, Gaetan, H.; 31 Stone Ridge Lane, Branford, CT 06405 (US). COOK, James, H., II; 36 Mallard Cove, East Hampton, CT 06424 (US). LEASE, Timothy, G.; 74 Christopher Lane, Guilford, CT 06437 (US). WOLANIN, Donald, J.; 320 Longmeadow Road, Orange, CT 06477  |           | (US). KRAMSS, Richard, H.; 978 Little Meadow Road, Guilford, CT 06437 (US). HERTZOG, Donald, L.; 421 Warpas Road, Madison, CT 06443 (US). OSTERHOUT, Martin, H.; Apartment 11, 409 Whitney Avenue, New Haven, CT 06511 (US).<br><b>(74) Agents:</b> GRAY, William, F. et al.; Bayer Corporation, 400 Morgan Lane, West Haven, CT 06516 (US).<br><b>(81) Designated States:</b> AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).<br><b>Published</b><br><i>With international search report.</i><br><b>(88) Date of publication of the international search report:</b><br>11 November 1999 (11.11.99) |
| <b>(54) Title:</b> SUBSTITUTED PYRIDINES AND BIPHENYLS AS ANTI-HYPERCHOLESTERINEMIC, ANTI-HYPERLIPOPROTEINEMIC AND ANTI-HYPERGLYCEMIC AGENTS<br><b>(57) Abstract</b><br><p>Substituted pyridines of formula (IA) are produced by reaction of suitably substituted pyridylaldehydes with Grignard or Witting reagents, and the resulting products are appropriately reduced. The pyridines of formula (IA) are suitable as active compounds in pharmaceutical products, particularly in pharmaceutical products for the inhibition of cholesterol ester transfer proteins. 3-Heteroalkyl-aryl-substituted pyridines of formula (IB) are produced from pyridines which are correspondingly protected at the hydroxy group and correspondingly substituted. The compounds of formula (IB) according to the invention are suitable as active compounds in pharmaceutical products, particularly pharmaceutical products for the treatment of hyperlipoproteinemia. Substituted pyridines and benzenes of formula (IC) are produced by procedures disclosed herein, and are useful as active ingredients in pharmaceutical products, particularly pharmaceutical products for inhibition of the glucagon receptor, leading to treatment of glucagon-mediated conditions such as diabetes.</p> |           |   |

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 97/13248

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C07D213/30 C07D213/32 C07D403/06 A61K31/44

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages           | Relevant to claim No. |
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| Y          | EP 0 325 129 A (BAYER AG) 26 July 1989<br>see claims 1-14<br>---                             | 1-47                  |
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|            | ---<br>-/--  |                       |



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

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Date of the actual completion of the international search

24 February 1998

Date of mailing of the international search report

06.03.98

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|------------|---|-----------------------|
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# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 97/13248

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

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2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
  
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## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
  
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Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: 1-10

anti-hypercholesterinemic tetrasubstituted 4-arylpyridines of formula IA having an alkyl group in 3- and/or 5-position which carries a cyclic moiety

2. Claims: 11-20

anti-hyperlipoproteinemic trisubstituted 3-hydroxymethyl-4-arylpyridines of formula IB having an heteroalkyl group in the 5-position which carries a cyclic moiety

3. Claims: 21-47

anti-glucemic tetrasubstituted 4-(het)arylpyridines and benzenes of formulae IA, IB, IC and ID having a hydroxy, trifluoroacetyl or alkyl group in the 5-position which is substituted by a trifluoromethyl or hydroxy group



# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 97/13248

| Patent document<br>cited in search report | Publication<br>date | Patent family<br>member(s) | Publication<br>date |
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